Amendments to the Specification:

1. Please replace the first paragraph on page 5 (lines 1-7) of the as-filed application with the following amended paragraph:

Anti-hypertensive agents lower blood pressure. There are many different categories of anti-hypertensive agents including calcium channel blockers, angiotensin converting enzyme inhibitors (ACE inhibitors), angiotensin II receptor antagonists (A-II antagonists), diuretics, beta-adrenergic receptor blockers (beta-blockers), vasodilators, and alpha-adrenergic receptor blockers (alpha-blockers). One example of a beta-blocker is ~~Propanolol~~ propranolol or a derivative thereof. One example of a vasodilator is Sodium Nitroprusside or a derivative thereof.

2. Please replace the fourth paragraph on page 6 (lines 10-12) of the as-filed application with the following amended paragraph:

Figure 3c is a photograph of a histological section of muscle tissue from rats 4 days after intravenous administration of CA-4DP at 100mg/kg where the rats were pretreated with ~~propanolol~~propranolol.

3. Please replace the last paragraph on page 6 (lines 20-31) of the as-filed application with the following amended paragraph:

A conventional Beta-adrenergic blocking agent ("Beta blocker") is used as a prophylactic or interventional therapeutic agent to prevent or treat VTA-associated acute hypertension or cardiotoxicity in an animal patient. The preferred Beta blocker is ~~Propanolol Hydrochloride~~propranolol hydrochloride which is available for use in clinical patients as oral or injectable formulations (Inderal®; Wyeth-Ayerst, Philadelphia, PA) or as a sustained-release capsule (Inderal®LA (Wyeth Ayerst, Philadelphia, PA). Other Beta blockers include oral formulations of Timolol Maleate (BLOCADREN®; Merck& Co., West Point, PA), Carteolol Hydrochloride (CARTROL® ; Abbott Laboratories, Abbott Park, IL); Carvedilol (COREG®; SmithKline Beecham Pharmaceuticals, Philadelphia, PA), Betaxolol Hydrochloride (KERLONE®; G.D. Searle& Co., Chicago, IL), 1-(tert-butyl-amino)3-[(5,6,7,8-tetrahydro-cis-

6,7-dihydroxy-1-naphthyl)oxy]-2-propanolol (Nadolol; Mylan Pharmaceuticals Inc., Morgantown, WV), Labetalol Hydrochloride

4. Please replace the fourth paragraph on page 16 (lines 21-28) of the as-filed application with the following amended paragraph:

In a separate group of rats (n=4), the beta blocker DL-~~Propanolol~~propranolol (1-[ispropylamino]3-[1-napthyloxy]-2-propanol hydrocholoride; Sigma-Aldrich Co., St. Louis MS) was administered by continual i.v. infusion into the venal cannula at rate of 20ug/kg/min. As demonstrated in Figure 1, the infusion of ~~Propanolol~~propranolol just prior to dosing with 30mg/kg CA-4P prevented the dramatic increase in blood pressure seen in CA-4DP-treated rats. Instead, MABP was stabilized within 5-10mmHg of control levels and maintained at that level for the course of 2 hours. Saline control alone had no effect on controlling CA-4DP-induced increase in MABP (data not shown).

5. Please replace the last paragraph beginning on page 16, line 29 and continuing through page 17, line 3 of the as-filed application with the following amended paragraph:

In contrast to ~~Propanolol~~propranolol treatment, the vasodilator Sodium Nitroprusside Dihydrate ("SNP", sodium nitroferricyanide; Sigma-Aldrich Co., St. Louis, MS) was administered subsequent to CA-4DP treatment (30mg/kg). SNP was infused (20 ug/kg/min) at the first sign of an increase in MABP. As Figure 1 again demonstrates, this led to prolonged stabilization of MABP, similar to that observed with ~~Propanolol~~propranolol. When the infusion was stopped, however, MABP rose sharply in all treated rats.

6. Please replace the fourth paragraph on page 17 (lines 24-28) of the as-filed specification with the following amended paragraph:

As in Example 1, MABP was continuously monitored via the tail artery cannula following dosing with CA-4DP (i.p., 30 mg/kg) or Saline. Separate treatment groups were infused with SNP, ~~propanolol~~propranolol, or saline. ~~Propanolol~~Propranolol was administered before CA-4DP treatment while SNP infusions were started only when the MABP began to rise in CA-4DP-treated rats.

7. Please replace the third paragraph on page 18 (lines 11-21) of the as-filed specification with the following amended paragraph:

Figure 2a illustrates the MABP in each treatment group 1 hour after CA-4DP or control dosing and just prior to TBF assay. CA-4DP increased MABP 72% from 7.2 mmHg in control animals (n=6 animals) to 107.9 mmHg. Co-administration of SNP (n=6) or ~~propanolol~~propranolol (n=5) reduced MABP to Saline control levels (82.7 and 80.2 mmHg respectively). As in the previous example, MABP after CA-4DP alone is significantly higher than for any other group. Heart Rate was also measured in treated animals at 1hour post-CA-4DP dosing. This value was calculated from the peak frequency from the MABP measurements. Figure 2c demonstrates that Heart Rate was significantly reduced in CA-4DP-treated rats (265.6 bpm, n=5) relative to saline control and this effect was also observed with co-administration of ~~propanolol~~propranolol (248.5 bpm, n=5). However, SNP removed this effect and returned the heart rate to normal levels (414.4 bpm, n=5).

8. Please replace the last paragraph on page 18 (lines 22-27) of the as-filed specification with the following amended paragraph:

As Figure 2b demonstrates, CA-4DP has dramatic effects on blood flow to tumor tissue. Co-administration of an anti-hypertensive does not significantly alter the magnitude of these effects. Approximately 1 hour after treatment, TBF was reduced to 14% of saline control in rats treated with CA-4DP only, while co-administration of SNP or ~~propanolol~~propranolol caused a reduction in tumor blood flow of 12.6 and 7.6% of control respectively.

9. Please replace the title of Example 3 on page 19, lines 2-3 of the as-filed specification with the following amended title:

EFFECT OF SINGLE DOSE VTA ON HEART TISSUE AND THE PROTECTIVE EFFECTS OF ~~PROPANOLOL~~PROPRANOLOL

10. Please replace the last paragraph on beginning on page 19 (line 29) through page 20 (line 8) of the as-filed specification with the following amended paragraph:

To investigate the cardiac protective properties of an antihypertensive agent, another group of rats (n=6) were pretreated with 2mg/kg ~~Propanolol~~ Propranolol Hydrochloride (INDERAL®, Wyeth-Ayerst, Philadelphia, PA) at 1 hour prior to administration of CA-4DP

(100mg/kg). With pretreatment of ~~propanolol~~propranolol, the adverse effects of ~~propanolol~~propranolol were observed to be minimized, with less or no hyalinization in the myocytes. There was no abnormal CA-4DP-related histopathology at either 6 or 24 hours post-treatment and no evidence of an increase in total number of visible myocardial cells, no evidence of neutrophil or macrophage infiltration, necrosis, or abnormal myofibers. Figure 3c demonstrates that cardiac tissue remained healthy even after 4 days of CA-4DP treatment. These observations are consistent with a cardioprotective effect of anti-hypertensive agents which counteracts any cardiotoxic side effects of vascular targeting agents.

11. Please replace the fourth paragraph on page 4 (lines 23-26) of the as-filed specification with the following amended paragraph:

Vascular targeting agents are anti-angiogenic agents. Anti-angiogenic agents inhibit the growth and maintenance of new blood vessels. Other categories of anti-angiogenic agents include, agents which inhibit the action of growth factors and anti-invasive agents.

12. Please replace the fifth paragraph on page 12 (lines 22-25) of the as-filed specification with the following amended paragraph:

Pharmaceutical compositions of the invention are formulated to be compatible with its intended route of administration. Pharmaceutical compositions [[str]]are prepared from the active ingredients or their salts in combination with pharmaceutically acceptable carriers.